BLOOD TRANSFUSION IN ELDERLY PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

WEN-CHIH WU, M.D., SAIF S. RATHORE, M.P.H., YONGFEI WANG, M.S., MARTHA J. RADFORD, M.D., AND HARLAN M. KRUMHOLZ, M.D.

ABSTRACT

Background Anemia may have adverse effects in patients with coronary artery disease. However, the benefit of blood transfusion in elderly patients with acute myocardial infarction and various degrees of anemia is uncertain.

Methods We conducted a retrospective study of data on 78,974 Medicare beneficiaries 65 years old or older who were hospitalized with acute myocardial infarction. Patients were categorized according to the hematocrit on admission (5.0 to 24.0 percent, 24.1 to 27.0 percent, 27.1 to 30.0 percent, 30.1 to 33.0 percent, 33.1 to 36.0 percent, 36.1 to 39.0 percent, or 39.1 to 48.0 percent), and data were evaluated to determine whether there was an association between the use of transfusion and 30-day mortality.

Results Patients with lower hematocrit values on admission had higher 30-day mortality rates. Blood transfusion was associated with a reduction in 30-day mortality among patients whose hematocrit on admission fell into the categories ranging from 5.0 to 24.0 percent (adjusted odds ratio, 0.22; 95 percent confidence interval, 0.11 to 0.45) to 30.1 to 33.0 percent (adjusted odds ratio, 0.69; 95 percent confidence interval, 0.53 to 0.89). It was not associated with a reduction in 30-day mortality among those whose hematocrit values fell in the higher ranges. In one of seven subgroup analyses (among patients who survived at least two days), transfusion was not associated with a reduction in mortality for patients with hematocrit values of 30.1 percent or higher.

Conclusions Blood transfusion is associated with a lower short-term mortality rate among elderly patients with acute myocardial infarction if the hematocrit on admission is 30.0 percent or lower and may be effective in patients with a hematocrit as high as 33.0 percent on admission. (N Engl J Med 2001;345:1230-6.)

ANEMIA is common in the elderly, occurring in 24 to 40 percent of hospitalized patients older than 65 years of age.[1,2] Although patients with anemia who have coronary artery disease or risk factors for coronary disease have an increased risk of death in the short term,[3,4] the prognostic importance of anemia in patients who present with acute myocardial infarction is not well defined. Furthermore, there is uncertainty concerning the appropriate role of blood transfusion. Whereas the effectiveness of blood transfusion in patients with gastrointestinal hemorrhage,[5] in patients undergoing cardiac[6] and noncardiac[7] surgery, and in critically ill patients[8] is known, its role in patients with acute coronary syndromes is inadequately characterized.[9] Current recommendations are based primarily on expert opinion, rather than on published evidence.[10-12] We sought to determine the risk associated with anemia in patients with acute myocardial infarction and the effectiveness of blood transfusion in a national cohort of elderly patients hospitalized with acute myocardial infarction.

METHODS

The Cooperative Cardiovascular Project

The Cooperative Cardiovascular Project (CCP) has been described in detail elsewhere.[13] Briefly, the CCP was a national program of the Health Care Financing Administration (currently the Centers for Medicare and Medicaid Services) that was developed to improve the quality of care for Medicare beneficiaries with acute myocardial infarction. The 234,769 patients in the CCP cohort constitute a sample of beneficiaries of the fee-for-service program of Medicare who were discharged from nongovernmental acute care hospitals in the United States with a primary diagnosis at discharge of acute myocardial infarction (code 410 of the *International Classification of Diseases, 9th Revision, Clinical Modification* [ICD-9-CM]) between January 1994 and February 1995, excluding patients for whom the hospitalization had been a readmission for acute myocardial infarction (ICD-9-CM code 410.x2).[14]

Study Sample

Our cohort was restricted to patients 65 years of age or older who were hospitalized with confirmed acute myocardial infarction.[13] We therefore excluded 17,593 patients younger than 65 years of age, 45,349 patients who did not have confirmed acute myocardial infarction on admission, and 23,773 patients who had been readmitted for acute myocardial infarction. We also excluded 42,278 patients who had been transferred to the study hospital and 39,028 patients who were transferred from the study hospital to another hospital, because we were unable to evaluate their full hospital course. Since the principal focus of our analysis was the prognostic importance of anemia complicating acute myocardial infarction and the way in which transfusion modifies the risk of death, we excluded 12,453 patients who had a hematocrit above the upper limit of normal (48 percent)[15] on admission, 11,799 patients for whom no data were available on the hematocrit on admission, and 65 patients with implausible hematocrit values (lower than 5 percent) on admission. We also excluded 4617 patients who had a documented terminal illness or metastatic cancer, 46,235 patients who had bleeding or hemorrhage within 48 hours before their hospitalization or while they were hospitalized, and 20,724 patients who un-

From the Division of Cardiovascular Diseases, Brown University Medical School, Providence, R.I. (W.-C.W.); the Section of Cardiovascular Medicine, Department of Medicine (S.S.R., Y.W., M.J.R., H.M.K.), and the Section of Health Policy and Administration, Department of Epidemiology and Public Health (H.M.K.), Yale University School of Medicine, and Yale–New Haven Hospital Center for Outcomes Research and Evaluation (M.J.R., H.M.K.) — both in New Haven, Conn.; and Qualidigm, Middletown, Conn. (M.J.R., H.M.K.).

derwent open-heart surgery, including coronary-artery bypass grafting, because of the presence of alternative clinical indications for the use or withholding of blood transfusion. We also excluded 325 patients whose vital status could not be verified and 77 patients whose date of discharge fell outside the study period. In total, 155,795 of the original 234,769 patients (66.4 percent) met one or more criteria for exclusion; the 78,974 remaining patients (33.6 percent) constituted the study cohort.

Hematocrit Value on Admission

Patients' hematocrit values on admission (the first measurement taken within 24 hours after arrival at the hospital) were divided into seven categories — 5.0 to 24.0 percent, 24.1 to 27.0 percent, 27.1 to 30.0 percent, 30.1 to 33.0 percent, 33.1 to 36.0 percent, 36.1 to 39.0 percent, and 39.1 to 48.0 percent — for the purpose of evaluating the associations among the hematocrit on admission, various characteristics of the patient, and outcomes. Anemia was defined according to the criteria of the World Health Organization[16] by a hematocrit value on admission of less than 39 percent.

Blood Transfusion, In-Hospital Outcomes, and 30-Day Mortality

We classified patients as having received a transfusion if they received whole blood or packed red cells at any point during their hospitalization. The principal outcome was death within 30 days after admission as ascertained from the Medicare Enrollment Database.[17] In addition, we evaluated patients for in-hospital outcomes, including the development of congestive heart failure, the occurrence of shock, and length of hospitalization.

Statistical Analysis

We first sought to determine the distribution of hematocrit values on admission among elderly patients hospitalized with myocardial infarction. The categories of hematocrit values were evaluated for univariate associations with the demographic and clinical characteristics of the patients. Continuous variables for which less than 10 percent of data were missing had the missing data replaced by median values; 0.6 percent of patients had missing data on mean heart rate, 2.6 percent on arterial pressure, and 0.3 percent on white-cell count. Categorical variables for which less than 10 percent of observations were missing had the missing variables coded as "not present"; 0.5 percent of patients had missing data on whether they had been admitted from a nursing home, 4.0 percent on peripheral vascular disease, 4.0 percent on history of angina, 5.2 percent on ventricular tachycardia, 7.0 percent on congestive heart failure, 2.5 percent on continence, 2.9 percent on mobility, and 2.3 percent on renal insufficiency. Variables for which more than 10 percent of observations were missing were not evaluated.

In the second phase of our study, we evaluated the associations between the hematocrit value on admission and 30-day mortality by means of chi-square analysis. Kaplan–Meier survival curves were plotted for each group defined according to the hematocrit on admission.

The third phase of our study examined characteristics of the patients, the facilities, and the physicians and their associations with the use of transfusion during hospitalization. For patients, the characteristics we evaluated included demographic characteristics, medical history, clinical presentation, and laboratory and electrocardiographic findings at the time of admission. The characteristics of the facility that we considered included the type of cardiac care facilities available (no facilities for invasive cardiac procedures, a cardiac catheterization laboratory only, or facilities for coronary-artery bypass grafting), and the single characteristic of the physician that we considered was the specialty of the attending physician (cardiology, internal medicine, or other). The variables that were found by univariate analysis to be associated with the use of transfusion were incorporated into a stepwise logistic-regression model in which the use of transfusion was the dependent outcome. The model was refined by means of stepwise selection in which a P value of less than 0.005 was used as the criterion for inclusion in the model and a P value of more than 0.001 was used as the criterion for removal from the model.

Finally, we used chi-square analysis to evaluate the association between blood transfusion and 30-day mortality among groups defined according to the hematocrit. Logistic-regression models were used to determine the independent reduction in the risk of death associated with the use of transfusion within each hematocrit category. The model used clinical predictors of 30-day mortality incorporated in the Medicare Mortality Prediction System score,[18] previously identified predictors of the use of blood transfusion, and the therapies for acute myocardial infarction (primary reperfusion therapy, aspirin, or beta-blockers) that were provided on admission. Each model adjusted for clustering of patients according to hospital.

We also applied logistic-regression models to seven modified cohorts to determine whether the estimated risks of death were particular to subgroups of patients. We repeated the analyses with the patients stratified according to age (65 to 74 years old, 75 to 84 years old, or 85 years old or older) and sex to determine the consistency of the effect among older patients, male patients, and female patients. We repeated the analyses after the exclusion of patients with do-not-resuscitate orders and patients who died on the first day of hospitalization. Similarly, in order to ensure that the effects associated with transfusion were not attributable to the characteristics of a particular clinical cohort, we repeated the analyses after the exclusion of patients in whom shock developed during hospitalization, those who were treated with thrombolytic agents or underwent primary angioplasty, and those who had a history of internal bleeding or a bleeding disorder. Since we could not determine when patients received their transfusions, it is conceivable that transfusion may appear to be effective because patients who did not receive a transfusion died before they were able to receive one. We therefore repeated the analyses excluding the patients who died within two days after admission.

All reported P values are two-sided. Analyses were performed with the use of SAS software (version 6.12, SAS Institute, Cary, N.C.) and Stata software (version 6.0, Stata, College Station, Tex.).

RESULTS

Of the 78,974 patients in the study cohort, 34,275 (43.4 percent) had a hematocrit of 39.0 percent or lower on admission; 3324 of the patients in the cohort (4.2 percent) had a hematocrit of 30.0 percent or lower on admission. Patients with lower hematocrit values on admission were more likely to have a history of internal bleeding, to have recently undergone surgery or to have had trauma, and to have more coexisting conditions. They were also more likely to present with cardiac arrest or shock, to have a do-not-resuscitate order, to have a higher heart rate, and to have lower mean arterial pressure and were less likely to have infarctions with ST-segment elevation. Primary reperfusion, beta-blockers, and aspirin were used less frequently in patients with lower hematocrit values on admission (Table 1).

Lower hematocrit values were associated with more frequent in-hospital events, including shock, heart failure, and death, and with an increased length of stay (Table 2). Crude 30-day mortality rates were highest among the patients whose hematocrit values on admission were in the lowest category and steadily declined with increasing hematocrit values (Fig. 1).

A total of 3680 patients (4.7 percent) received a blood transfusion during hospitalization. The rate of

TABLE 1. CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	HEMATOCRIT ON ADMISSION							ALL PATIENTS (N=78,974)
	5.0–24.0% (N=380)	24.1–27.0% (N=838)	27.1–30.0% (N=2106)	30.1–33.0% (N=4848)	33.1–36.0% (N=9885)	36.1–39.0% (N=16,218)	39.1–48.0% (N=44,699)	
Age (yr)	79.5±8.2	79.2±7.8	79.5±7.8	80.1±7.7	79.7±7.6	78.8±7.6	76.7±7.4	77.8±7.6
Female sex (%)	58.7	63.8	63.0	65.6	67.7	64.5	45.4	54.1
White race (%)	83.2	80.2	84.0	84.3	87.0	88.6	91.4	89.5
Medical history (%)								
Active ulcer disease	13.7	11.7	13.6	13.9	12.8	12.8	12.2	12.6
History of internal bleeding	17.6	10.7	12.0	10.2	8.5	7.3	6.4	7.3
Recent trauma, surgery, or biopsy	9.0	10.3	9.9	8.9	7.6	6.3	4.3	5.7
Peripheral vascular disease	15.0	13.6	16.2	14.1	11.8	10.8	9.5	10.6
Cigarette smoking	10.3	9.6	9.9	9.1	9.3	10.9	14.9	12.8
History of cerebrovascular disease or stroke	16.6	17.8	18.7	17.6	16.5	16.1	14.6	15.5
History of myocardial infarction†	30.0	26.0	31.4	31.7	31.4	30.0	30.0	30.3
History of angina	42.6	40.5	43.0	43.5	45.1	46.0	44.9	45.0
CABG	9.5	11.0	12.6	12.8	12.4	12.9	14.4	13.6
PTCA	5.3	5.4	5.8	4.8	5.8	6.1	6.1	6.0
Clinical presentation								
Cardiac arrest (%)	7.1	7.6	6.4	4.7	4.2	3.5	3.1	3.6
Shock (%)	5.8	5.5	4.4	3.4	3.1	2.4	1.9	2.4
Persistent angina (%)	20.8	27.0	24.4	28.1	30.1	33.6	36.6	34.1
Ventricular tachycardia (%)†	1.1	0.7	1.0	0.8	1.0	0.7	0.9	0.9
Infarction with ST-segment elevation (%)	19.0	22.4	22.6	24.5	25.9	27.4	30.0	28.3
Congestive heart failure (%)	48.4	48.6	44.0	41.3	35.4	30.2	27.2	30.4
Subendocardial infarction (%)	41.8	45.5	45.7	43.8	42.8	41.7	39.3	40.7
APACHE II score‡	13.0±5.7	12.9±5.9	12.2±5.5	11.3±5.3	10.3±4.9	9.6±4.7	9.5±4.6	9.9±4.8
Arterial pressure (mm Hg)	91.0±22.7	92.6±22.4	94.4±22.2	95.9±21.2	97.3±21.0	100.3±20.5	104.7±20.9	101.9±21.2
Heart rate (bpm)	92.0±21.1	91.7±23.6	90.2±23.8	89.8±24.3	88.7±24.7	87.7±24.1	88.7±24.7	88.6±24.5
White-cell count (per mm^3)	12,600± 8,400	11,400± 6,900	11,400± 5,900	10,900± 5,400	10,800± 5,200	10,700± 4,700	11,000± 4,700	10,900± 4,900
Coexisting conditions (%)								
Limited mobility	39.0	41.2	39.6	37.2	32.2	26.2	20.2	24.8
Diabetes	34.0	40.7	40.7	36.2	32.8	31.0	30.4	31.6
COPD	18.2	19.2	20.2	19.5	19.3	19.2	21.1	20.3
Renal insufficiency	45.3	51.6	42.3	29.9	18.4	10.5	5.6	11.4
Hypertension	56.6	65.4	64.5	65.9	64.4	62.8	60.7	62.0
Do-not-resuscitate order (%)	22.1	20.4	19.5	16.8	14.0	11.7	8.8	11.0
Hospital facilities for cardiac care (%)								
CABG suite	36.1	40.3	34.3	37.1	37.6	37.6	39.3	38.4
Catheterization laboratory only	25.5	19.3	24.6	22.8	22.3	22.3	21.9	22.2
No facilities for invasive procedures	38.4	40.3	41.1	40.1	40.1	40.2	38.8	39.4
Treated by a cardiologist (%)	19.7	22.4	23.1	25.2	28.0	29.8	33.2	30.9
Treatment during hospitalization (%)								
Aspirin on admission	49.7	57.8	61.1	67.6	72.8	76.4	80.3	76.9
Beta-blockers on admission	23.4	27.3	28.5	33.5	38.1	42.6	46.8	43.2
Primary reperfusion therapy	5.3	4.3	5.3	7.4	8.9	12.3	17.3	14.1
Cardiac catheterization	9.7	10.4	10.5	14.6	18.2	22.8	29.4	24.9
PTCA	4.2	3.1	4.8	5.8	7.3	9.0	12.3	10.3

*Plus–minus values are means ±SD. CABG denotes coronary-artery bypass grafting, PTCA percutaneous transluminal coronary angioplasty, and COPD chronic obstructive pulmonary disease.

†$P>0.05$ for trend; all other trends were significant at $P\leq 0.05$.

‡Higher scores on the Acute Physiology and Chronic Health Evaluation (APACHE II) indicate more severe illness.

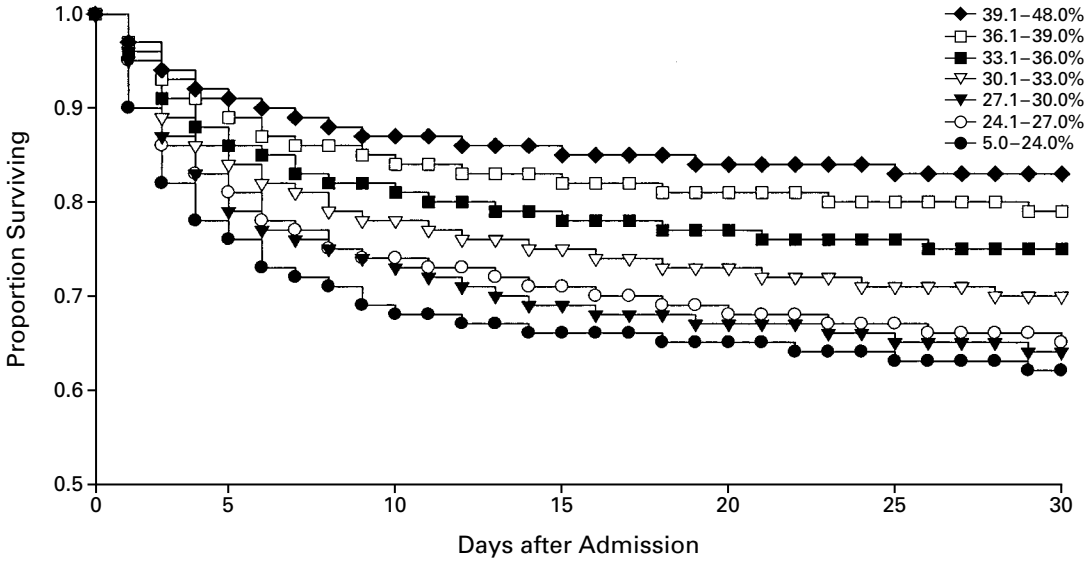
use of transfusion was highest (71.3 percent) among patients with the lowest hematocrit values on admission (5.0 to 24.0 percent) and steadily decreased with higher hematocrit values (Table 2). Independent predictors of the use of transfusion in this cohort were female sex (odds ratio for the use of transfusion, 1.65), history of internal bleeding (odds ratio, 1.63), previous angioplasty (odds ratio, 1.27), recent trauma or surgery (odds ratio, 1.68), renal insufficiency (odds ratio, 3.28), peripheral vascular disease (odds ratio, 1.25), a higher score on the Acute Physiology and Chronic Health Evaluation (APACHE II) (odds ratio, 1.04 per increase of 1 point), a mean arterial pressure of less than 70 mm Hg (odds ratio, 1.52), congestive heart failure (odds ratio, 1.27), the type of hospital cardiac care facilities (odds ratio, 1.22 for hospitals

TABLE 2. HOSPITAL COURSE AND MORTALITY RATE.*

CHARACTERISTIC	HEMATOCRIT ON ADMISSION							ALL PATIENTS (N=78,974)	P VALUE FOR TREND
	5.0–24.0% (N=380)	24.1–27.0% (N=838)	27.1–30.0% (N=2106)	30.1–33.0% (N=4848)	33.1–36.0% (N=9885)	36.1–39.0% (N=16,218)	39.1–48.0% (N=44,699)		
Length of stay (days)†	9.9±7.4	10.6±8.8	10.0±6.4	9.6±6.1	9.1±7.5	8.6±5.5	8.3±4.6	8.6±5.4	<0.001
In-hospital events (%)									
Shock	15.0	10.3	10.9	9.5	8.6	7.5	6.2	7.2	<0.001
Heart failure	61.1	63.0	63.0	58.3	51.6	45.1	40.5	44.8	<0.001
Blood transfusion	71.3	53.6	30.2	12.6	5.6	2.8	1.6	4.7	<0.001
Mortality (%)									
In-hospital	33.2	30.3	31.2	25.7	21.7	17.6	14.6	17.5	<0.001
30-Day	38.7	35.2	35.9	30.0	25.6	20.9	17.2	20.6	<0.001

*Plus–minus values are means ±SD.

†The assessment of the length of stay excluded patients who died during the hospitalization.



HEMATOCRIT CATEGORY	no. (%) at risk						
5.0–24.0%	380 (100.0)	277 (72.9)	257 (67.6)	250 (65.8)	247 (65.0)	240 (63.2)	233 (61.3)
24.1–27.0%	838 (100.0)	655 (78.2)	611 (72.9)	587 (70.0)	570 (68.0)	557 (66.5)	543 (64.8)
27.1–30.0%	2,106 (100.0)	1,618 (76.8)	1,507 (71.6)	1,442 (68.5)	1,405 (66.7)	1,375 (65.3)	1,350 (64.1)
30.1–33.0%	4,848 (100.0)	3,972 (81.9)	3,727 (76.9)	3,597 (74.2)	3,508 (72.4)	3,437 (70.9)	3,392 (70.0)
33.1–36.0%	9,885 (100.0)	8,382 (84.8)	7,938 (80.3)	7,692 (77.8)	7,559 (76.5)	7,456 (75.4)	7,353 (74.4)
36.1–39.0%	16,218 (100.0)	14,176 (87.4)	13,589 (83.8)	13,294 (82.0)	13,091 (80.7)	12,950 (79.8)	12,825 (79.1)
39.1–48.0%	44,699 (100.0)	40,132 (89.8)	38,670 (86.5)	38,007 (85.0)	37,544 (84.0)	37,267 (83.4)	37,002 (82.8)

Figure 1. Kaplan–Meier 30-Day Survival Curves According to Hematocrit Category.

with a cardiac catheterization laboratory; odds ratio, 1.48 for hospitals with facilities for coronary-artery bypass grafting; and odds ratio, 1.00 for hospitals with no facilities for invasive cardiac care [the reference category]), the specialty of the physician (odds ratio, 1.08 for cardiologists; odds ratio, 1.25 for family physicians; and odds ratio, 1.00 for internists [the reference category]), the use of beta-blockers (odds ratio, 1.13), and the use of primary reperfusion therapy on admission (odds ratio, 1.62). Patients were less likely to receive a transfusion if they were white (odds ratio, 0.79), had cardiac arrest (odds ratio, 0.69), had a do-not-resusci-

tate order (odds ratio, 0.70), or had been admitted from a nursing home (odds ratio, 0.80).

The association between transfusion and outcomes varied substantially according to the patient's hematocrit on admission. Transfusion was associated with lower 30-day mortality among patients whose hematocrit values on admission were 33.0 percent or lower but with increased 30-day mortality for patients whose values were 36.1 percent or higher.

With or without adjustment for multiple variables, the odds ratio for death among patients who received a transfusion steadily increased with the admission hematocrit value; the odds ratio was below 1.00 for patients with hematocrit values of 33.0 percent or lower and above 1.00 for patients with hematocrit values higher than 33.0 percent (Table 3). Additional analyses indicated that the effectiveness of blood transfusion was similar among patients with hematocrit levels of 33.0 percent or lower when stratified according to age or sex, as well as in the subgroups that excluded patients who received primary reperfusion therapy, those in whom shock developed during hospitalization, those who had a history of internal bleeding or a bleeding disorder, those with do-not-resuscitate orders, or those who died on the first day of hospitalization.

The exclusion of the patients who died within two days after admission eliminated the survival benefit associated with transfusion among patients with a hematocrit level between 30.1 percent and 33.0 percent (odds ratio, 0.98; 95 percent confidence interval, 0.76 to 1.25). However, transfusion was still associated with a reduction in mortality among patients with a hematocrit level of 24.0 percent or lower (odds ratio, 0.36; 95 percent confidence interval, 0.15 to 0.83), those with a hematocrit level between 24.1 percent and 27.0 percent (odds ratio, 0.69; 95 percent confidence interval, 0.47 to 1.01), and those with a hematocrit level between 27.1 percent and 30.0 percent (odds ratio, 0.75; 95 percent confidence interval, 0.58 to 0.96).

TABLE 3. ASSOCIATION OF BLOOD TRANSFUSION WITH 30-DAY MORTALITY, ACCORDING TO HEMATOCRIT CATEGORY.

HEMATOCRIT CATEGORY	ODDS RATIO (95% CI) FOR DEATH WITHIN 30 DAYS*		
	UNADJUSTED	WITH ADJUSTMENT FOR CLINICAL FACTORS†	WITH ADJUSTMENT FOR CLINICAL FACTORS, MEDICATION USE, AND PREDICTORS OF TRANSFUSION‡
5.0–24.0%	0.37 (0.23–0.59)	0.31 (0.17–0.55)	0.22 (0.11–0.45)
24.1–27.0%	0.42 (0.31–0.56)	0.48 (0.34–0.66)	0.48 (0.34–0.69)
27.1–30.0%	0.49 (0.40–0.61)	0.54 (0.43–0.69)	0.60 (0.47–0.76)
30.1–33.0%	0.62 (0.51–0.76)	0.64 (0.50–0.82)	0.69 (0.53–0.89)
33.1–36.0%	1.01 (0.83–1.23)	1.05 (0.82–1.32)	1.13 (0.89–1.44)
36.1–39.0%	1.43 (1.16–1.77)	1.25 (0.96–1.64)	1.38 (1.05–1.80)
39.1–48.0%	1.66 (1.40–1.97)	1.40 (1.13–1.72)	1.46 (1.18–1.81)

*The odds ratios and 95 percent confidence intervals (CI) are for patients who received a blood transfusion as compared with those who did not.

†The analysis was adjusted for the score on the Acute Physiology and Chronic Health Evaluation (APACHE II), the presence or absence of a do-not-resuscitate order on admission, the location of the myocardial infarction, the presence or absence of congestive heart failure, the mean arterial pressure, the heart rate, and the presence or absence of renal insufficiency.

‡The analysis was adjusted for the variables used in the clinical adjustment plus the use or nonuse of primary reperfusion therapy, the use or nonuse of aspirin on admission, the use or nonuse of beta-blockers on admission, and predictors of the use of blood transfusion.

DISCUSSION

Our data indicate a high prevalence of anemia among elderly patients with acute myocardial infarction. In addition, we found that patients with anemia had a higher 30-day mortality rate than nonanemic patients. Our data suggest that blood transfusion is effective in reducing the short-term mortality rate among elderly patients with anemia who have acute myocardial infarction if their hematocrit on admission is 30.0 percent or lower and may be effective for patients with hematocrit levels as high as 33.0 percent.

The prevalence of anemia in our cohort was markedly higher than the prevalence of 5 to 20 percent observed in other studies[19-21] but is similar to estimates in other elderly populations without acute myocardial infarction.[1,2,22] The large number of patients with anemia highlights the need for data to guide treatment, especially because there are substantial variations among hospitals in the rate of use of blood transfusion.[23,24] The 4.7 percent rate of use of transfusion in the CCP is similar to the 5.4 percent rate reported among patients with cardiac conditions at county hospitals in Minnesota[25] and the 6.0 percent rate reported for elderly patients in a German university hospital.[26] However, rates of use of transfusion in other hospital surveys,[27] clinical trials,[19,28] and series in cardiac intensive care units[4] vary from 0.2 percent to 27.0 percent. The high degree of variability in the rate of use of transfusion is attributable to several factors, including the lack of uniform criteria for transfusion in patients with coronary disease, the varying types and severity of cardiac and noncardiac disease in different study populations, and variability in other characteristics of the patients enrolled in studies of the use of transfusion. Although the rates of use vary, studies consistently indicate a high rate of use of transfusion among patients with ischemic heart disease, with such patients accounting for as much as 14.3 percent of all transfusions performed.[29]

Previous analyses have provided contradictory findings regarding the ideal hematocrit threshold at which to initiate therapy. Studies in humans and animals have shown that healthy hearts have a remarkable tolerance for low hematocrit values (below 15 percent).[30-32] Nonetheless, compensatory mechanisms in patients with low hematocrit values involve a decrease in the

coronary reserve, caused by an increase in the blood flow at rest and a redistribution of the blood flow away from the endocardium.[30,31,33] Hébert and colleagues found that short-term mortality was similar in patients with noncardiac problems who had hematocrit values of 27 percent after transfusion and in those who had hematocrit values of 36 percent after transfusion.[8,34] However, when coronary reserve is limited (for example, by coronary stenosis), manifestations of myocardial ischemia may occur with only mild anemia (a hematocrit of 20 to 30 percent).[35-37] In one study, the risk of death in the hospital among patients with cardiac disease was reduced when they were treated at pretransfusion hematocrit values as high as 37.5 percent.[4] In addition, studies in patients with anemia with and without concomitant renal insufficiency have suggested that treatment with epoetin may be beneficial in patients with heart failure, ischemic heart disease, or both when used to achieve hematocrit values of more than 30 percent.[38-40]

Confusion regarding the appropriate hematocrit levels at which to initiate transfusion is also evident in the published guidelines for blood transfusion,[11,12] only a few of which are directed toward the use of transfusion in nonsurgical patients.[10,41,42] The groups that have addressed the role of transfusion in such patients have uniformly agreed that transfusions should be given to patients with hematocrit values lower than 21 percent, with allowance for transfusion at higher hematocrit values in patients with coronary disease. However, these guidelines do not propose a specific value or range of values at which to consider transfusion for patients with cardiovascular disease, citing the lack of data to support recommendations for this population of patients.[10] Our findings address this deficiency by providing evidence of the effectiveness of transfusion in elderly patients with acute myocardial infarction whose hematocrit values are as high as 33.0 percent.

Although our study indicates that there is an overall benefit of transfusion in patients with acute myocardial infarction and anemia, patients who received transfusions despite the fact that their hematocrit values on admission were higher than 36.0 percent had a higher risk of death within 30 days than patients with similar hematocrit values who did not receive transfusions. Very few patients with hematocrit values in this category received transfusions, and we believe that the increased risk of death within 30 days is attributable to other events that occurred later during hospitalization, that were not measured by our analyses, and that were not associated with the hematocrit on admission. In any case, as expected on the basis of clinical experience and previous studies, we found no evidence that transfusion would be beneficial for patients with a hematocrit level greater than 33.0 percent.

Thus, our findings support the use of transfusion for elderly patients with anemia and acute myocardial infarction. The use of the CCP data base in our study allowed us to examine a large, broadly representative population of elderly patients with acute myocardial infarction and a wide spectrum of coexisting conditions, such as is rarely seen in randomized trials. Although this observational study cannot provide direct evidence of a relation among transfusion, improvement in the hematocrit, and outcome, our findings suggest that the judicious use of transfusion in elderly patients with myocardial infarction is associated with improved outcomes for patients with hematocrit levels of 30.0 percent or lower and may be effective in patients with a hematocrit level as high as 33.0 percent. Although a randomized, controlled trial would be useful to confirm the validity of this threshold for transfusion, it is unlikely that such a study will be conducted in the near future. In the interim, a more aggressive use of transfusion in the management of lower hematocrit levels in elderly patients with acute coronary disease may be warranted.

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